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A Comparison of Prospective and Retrospective Assessments of Diet in a Study of Colorectal Cancer

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Abstract: *Dietary factors are widely studied as risk factors for colorectal cancer, with much information from case-control studies. We evaluated the validity of dietary data from a retrospective case-control study of diet and colorectal cancer. As part of the α-Tocopherol, β-Carotene Cancer Prevention Study, diet was assessed at baseline and after diagnosis for colorectal cancer cases and at baseline and regularly during the trial for a random control group. The dietary assessment referred to the previous 12 months (in cases before diagnosis). In the two dietary assessments, the cases reported a greater increase in consumption of fruits and dairy products and a decrease in consumption of potatoes. Accordingly, relative risks for colorectal cancer by baseline dietary data differed markedly from odds ratios from case-control data; e.g., relative risk for a 652-mg increase in calcium intake was 0.79 (95% confidence interval = 0.48–1.30) in case-cohort analysis vs. an odds ratio of 1.57 (95% confidence interval = 1.06–2.33) for case-control analysis. The most likely explanation is the influence of current diet on recall of prediagnosis diet and effects of occult cancer on diet in the year before cancer diagnosis, which have implications for interpretation of case-control studies in evaluating associations between diet and colorectal cancer.*

Introduction

Colorectal cancer is, in the Western industrialized countries, one of the most common malignancies. In recent years research into risk factors has focused on diet; results have, however, been controversial (1). The most promising theory regarding diet and colorectal cancer involves the increased risk associated with high fat and meat consumption as well as low fiber intake (2). This theory is compatible with geographic variation in the risk for colorectal cancer, with time trends, and with migration studies (3).

Most information about diet and colorectal cancer comes from retrospective case-control studies in which dietary data have been collected after cancer diagnosis (4). Cancer patients are asked about their dietary habits during a specified time span before the onset of cancer symptoms, with controls asked about their dietary intake during a similar period (5,6). Many case-control studies on colorectal cancer have found a protective effect for high vegetable, fruit, and fiber intake (7), with high total energy intake and high dietary fat being related to an increased risk. The fact that fat intake is highly correlated with total energy intake, however, makes any specific association of these factors with cancer uncertain (8). Increased risks for colorectal cancer have also been observed from energy-adjusted intakes of protein and carbohydrates (9) and sugars (8).

In prospective studies, the associations between dietary factors and colorectal cancer have been inconsistent (4). Some studies have shown no association between the intake of meat, fat, or protein and colon cancer (10–12), whereas others have shown an elevated risk associated with high intake of red meat (13,14), processed meats (11,14), and animal fat (14). Even though high intake of fiber or vegetables has been proposed as being preventive for colorectal cancer, the cohort studies have not found a significant association (13–17).

The results of case-control studies may be especially prone to selection bias and differential recall between cases and controls. When the reliability of measuring food consumption retrospectively in cancer cases and controls has been assessed (5,6,18–23) for colorectal cancer patients or any cancer patients with advanced-stage disease, the difference between original and recall values has been larger than that for controls (5). Colorectal cancer patients may have changed their dietary habits as a result of their illness and, because of cancer-related stress, may have more difficulties in recalling their past diets (5,6). For subjects with unchanged food consumption, e.g., most controls, agreement between original and retrospective information has been good (6). Thus any consideration of recall bias should encompass the extent of different recall and the change in diet before diagnosis (24).

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By comparing changes in diet with time separately for cases and controls, conclusions can be drawn concerning the role of diet in the development of the disease: is it causal, or does the disease itself lead to changes in dietary habits or in the reporting of diet? The purpose of this study was to evaluate the validity of prediagnostic dietary data among colorectal cancer cases in estimating the risk between diet and colorectal cancer. We collected dietary data from colorectal cancer cases at least one year before diagnosis and again after diagnosis and similarly for random controls and compared the relative risks on the basis of baseline data and odds ratios from case-control data.

Materials and Methods

This study was done within the α-Tocopherol, β-Carotene Cancer Prevention (ATBC) Study (25), undertaken to test whether α-tocopherol or β-carotene supplementation could prevent lung cancer. Briefly, the participants of the ATBC Study (n = 29,133) were male smokers, recruited between 1985 and 1988 from the total male population, aged 50–69 years, of southwestern Finland (n = 290,406). The participants were randomly assigned to one of four supplementation groups: α-tocopherol alone (50 mg), α-tocopherol (50 mg) and β-carotene (20 mg), β-carotene alone (20 mg), or placebo. Before randomization the participants provided questionnaire data on their general background characteristics and medical, smoking, and dietary histories. Height and weight were measured. The follow-up consisted of three visits annually to the local study center. At these visits the men reported any illnesses and symptoms they had experienced, and each received a new capsule pack for the next period. The follow-up lasted for a median 6.1 years; the study ended on 30 April 1993.

Subjects

Cancer cases: Participants in the ATBC Study were asked to contact their local study center as soon as possible if they were diagnosed with cancer. If the cancer diagnosis was made over one year after study entry, an appointment for an extra visit, here called the case visit, was made. Two weeks before the case visit a dietary history questionnaire was sent to the participant to be completed at home and returned at the visit (the baseline procedure repeated; see **Dietary Assessment**). Only those cases still in the study at the time of cancer diagnosis were expected to respond to the request.

The study physicians reviewed centrally the medical records of all cancer cases for diagnostic confirmation, and in addition pathologists reviewed the original histopathological slides of the cancers. A total of 60 colorectal cancer cases were confirmed among the participants who attended the case visit, but inasmuch as 10 participants failed to complete the dietary questionnaire or returned it with insufficient data, 50 cases were acceptable for this analysis. All colorectal cancers were adenocarcinomas, except one carcinoma of the anorectal junction (cloacogenic carcinoma).

Figure 1 illustrates the flowchart of the cases for this analysis from the total of 129 colorectal cancers diagnosed in the ATBC Study after the first intervention year. Before diagnosis 45 colorectal cancer cases had already dropped out of the study and another 24 did not attend the case visit. Information about cancer for these cases was obtained later from the Finnish Cancer Registry, which covers 99% of colorectal cancers diagnosed in Finland (26).

Controls: A random sample (20%) of all the participants in each of the four supplementation groups was taken to assign controls at the beginning of the ATBC Study. The time

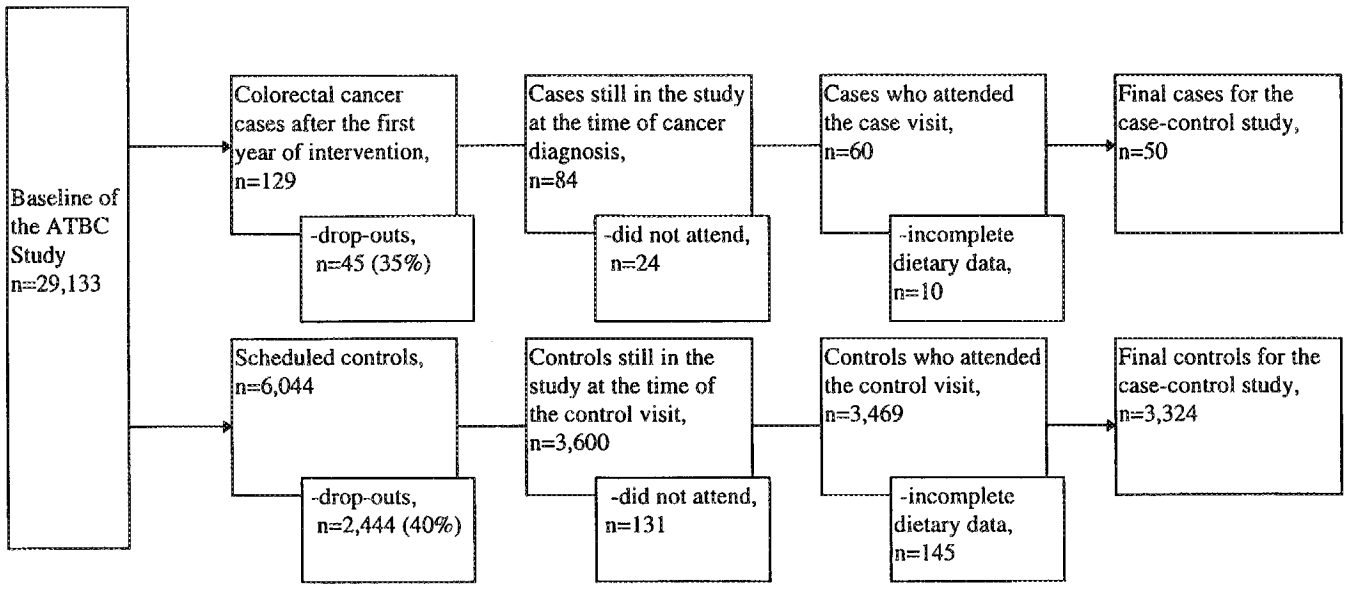

Figure 1. Selection of participants for study. ATBC Study, α-Tocopherol, β-Carotene Cancer Prevention Study.

of the follow-up visit, which was to be called the control visit, was determined at the beginning of the ATBC Study. These control visits were evenly allocated to all follow-up visits after the first intervention year. If a participant was still in the study at the time of his scheduled control visit and no cancer had been diagnosed, he was mailed a dietary history questionnaire two weeks before the visit (the same as at baseline; see **Dietary Assessment**).

Figure 1 shows the flowchart for forming the final group of controls. Of the 6,044 participants assigned as controls, 2,444 had dropped out of the study before the control visit and 131 did not attend the control visit even though they continued in the study. In addition, 145 participants failed to return the dietary questionnaire or returned it with insufficient data, leaving 3,324 of the controls for this analysis.

Dietary Assessment

The habitual diet was assessed by a self-administered modified dietary history method specifically designed and validated for the ATBC Study (27). The questionnaire included 276 food items and mixed dishes and was used together with a portion-size picture booklet with 122 photographs of foods, each with three to five different portion sizes. The participants were asked to report their usual frequency of food consumption and the usual portion size during the previous 12 months.

At the first baseline visit the questionnaire was given to all participants to be completed at home. The questionnaire was then reviewed with the study nurse at the second visit two weeks later. Finally, a coordinating center nutritionist reviewed the questionnaires and decided on approval. An acceptable questionnaire was obtained from 27,111 participants (93%) at baseline.

The same dietary questionnaire was sent to the cases and controls two weeks before the case-control visit. The cancer cases were asked to report their diet during the previous 12 months before the diagnosis. The questionnaire was reviewed with the study nurse at the visit and then later finally approved by a nutritionist. In some cases, information about a new cancer diagnosis emerged at a normal follow-up visit; in this case the dietary history questionnaire was given to the participant to be completed at home, and the participant mailed the questionnaire directly to the study coordinating center. Of the 50 cancer cases, one completed the questionnaire 39 days before colorectal surgery, but the other 49 cases completed the questionnaire after surgery [78 ± 63 (SD) days after surgery]. In addition to surgery, nine cases had received chemotherapy or radiation treatment before completing the questionnaire.

Statistical Analysis

We compared the change in food consumption and nutrient intake during follow-up between colorectal cancer cases and controls. This was done using an analysis of covariance model with the case or control visit dietary data as the response and baseline data, disease status (colorectal cancer case or control), and their interaction as the covariates. The effect of the baseline dietary data can be interpreted as the reliability of the dietary measurement, the effect of disease status as the recall bias, and their interaction as differential recall. We chose to test the disease status and the interaction jointly, inasmuch as either could corrupt the normal case-control estimation of risk. Adjustments were made for age at baseline and at the case-control visit (taking into consideration the follow-up time), for study supplementation group (α-tocopherol and/or β-carotene or placebo), and for total energy intake.

We calculated the relation between cancer risk and nutrient intake values of the 50 cases and 3,324 controls who had baseline and case-control dietary data. Case-control odds ratios were calculated with logistic regression (28) with case-control nutrient intake values as covariates. Adjustments were made for age and total energy intake at the case-control visit and for study supplementation group (α-tocopherol and/or β-carotene or placebo). The case-cohort relative risks were calculated with case-cohort analysis (29), with dietary data obtained at the baseline visit assumed to be unaffected by the undiagnosed cancer. The follow-up time was calculated from the day of recruitment to the day of the case-control visit. Adjustments were made for age and total energy intake at baseline and for the supplementation group.

Nutrient intakes, food consumption, and age were included in the models as continuous variables. We reran all analyses using logarithmic nutrient intake and food consumption values and obtained results similar to untransformed data. Thus the reported results are from analyses with continuous, untransformed values. Odds ratios and relative risks are presented per interquartile range for each nutrient, meaning the difference between the 25th and the 75th percentile. In all analyses we used the statistical package S-plus (30).

Results

Characteristics of Cases and Controls

Colorectal cancer cases were older than controls. At baseline the mean age of cases was 59 ± 5.9 (SD) years and at the case-control visit 63 ± 5.8 years and the age of controls was 57 ± 5.0 and 61 ± 5.2 years, respectively. Cases and controls were similar in their educational level and marital status. The body mass index decreased in cases during follow-up from a mean of 26.3 ± 3.6 to 25.7 ± 3.6 kg/m^2, but in controls it was 26.2 ± 3.7 and 26.4 ± 3.9 kg/m^2 at baseline and the control visit, respectively. The controls were evenly distributed among ATBC Study supplementation groups, but there were slightly more cases in the β-carotene group (32%) and slightly fewer taking α-tocopherol (20%). Study follow-up time from baseline to the case-control visit was

longer for cases than for controls: 1,502 ± 578 and 1,232 ± 577 days, respectively.

Case-Control Food Consumption and Change Over Time

At the case-control visit the cases reported on average a >10% higher consumption of cereals other than wheat or rye, fruits and berries, fruit juice, high-fat milk, low-fat milk, cream, cheese, sausage, margarine, and sugar but >10% lower consumption of coffee and sour milk products than controls (Table 1). Among the cases, the change in consumption of fruits and berries, fruit juice, low-fat milk, cream, cheese, red meat, egg, sugar, and potatoes during follow-up was significantly different from controls. After adjustment for age, follow-up time, and supplementation group, a significant difference remained between cases and controls for the change in consumption of these foods.

Case-Control Nutrient Intake and Change Over Time

At the case-control visit, total energy intake was significantly higher for cases than for controls (Table 2). This was due to their 13–16% higher intake of all energy-supplying nutrients (fat, protein, and carbohydrates) and was also reflected in their higher intake of other nutrients. From baseline, the intake of most nutrients had remained essentially unchanged among cases, except for sucrose, calcium, and vitamin D, the intake of which had increased. For controls, the intake of most nutrients decreased: the intake of protein and carbohydrates by 8% each and fat by 12%, leading to an 8% decrease in total energy intake. The difference between cases and controls in the change in intake of total energy, fat, protein, carbohydrates, cholesterol, and sucrose, as well as vitamin C and calcium, was statistically significant. After adjusting for total energy intake and age at baseline and at the case-control visit (taking into consideration the follow-up time), we found significant differences in the change in intake of starch, sucrose, fiber, vitamin C, calcium, and iron.

Relative Risks and Odds Ratios for Dietary Factors and Colorectal Cancer

The relative risks and odds ratios were calculated from the same group of individuals to allow us to compare the risk estimates over time. Relative risks and odds ratios for various dietary factors and colorectal cancer were considerably different when the baseline data (case-cohort design, relative risks) or case-control data (odds ratios) were used. Milk products in general, mainly low-fat milk, cheese, and ice cream, were associated with a significantly increased

Table 1. Daily Food Consumption at Case-Control Visit and Change in Daily Food Consumption From Baseline to Case-Control Visit[a]

Food	Case-Control Consumption		Change in Consumption		*P* Value for Δ[b]	
	Cases (n = 50)	Controls (n = 3,324)	Cases (n = 50)	Controls (n = 3,324)	Crude*	Adjusted†
Rye	79.9 ± 55.7	82.4 ± 59.1	−13.3 ± 64.2	−8.4 ± 58.9	0.42	0.41
Wheat	111 ± 59.4	101 ± 60.8	−5.0 ± 55.0	−6.7 ± 57.1	0.74	0.75
Other cereals[c]	23.9 ± 14.9	20.5 ± 16.6	3.3 ± 17.5	1.7 ± 15.3	0.08	0.10
Potatoes	164 ± 57.6	167 ± 73.2	−38.7 ± 83.8	−15.3 ± 74.1	0.02	0.03
Vegetables	114 ± 63.3	113 ± 70.7	5.8 ± 58.3	−6.5 ± 60.9	0.56	0.51
Fruits and berries	140 ± 104	121 ± 91.7	26.2 ± 95.9	−7.6 ± 89.9	0.04	0.04
Fruit juice	47.5 ± 123	26.7 ± 72.0	35.0 ± 115	1.5 ± 79.6	<0.01	<0.01
High-fat milk	166 ± 260	129 ± 250	−59.8 ± 273	−64.8 ± 238	0.58	0.55
Low-fat milk	465 ± 373	352 ± 298	115 ± 282	−4.8 ± 270	<0.01	<0.01
Sour milk[d]	89.3 ± 141	110 ± 177	−56.5 ± 176	−48.5 ± 190	0.60	0.69
Cream	18.0 ± 24.9	13.6 ± 19.9	1.0 ± 15.9	−2.6 ± 17.9	<0.01	<0.01
Cheese	37.3 ± 47.3	26.3 ± 29.5	14.0 ± 41.9	1.0 ± 30.0	<0.01	<0.01
Butter	27.2 ± 27.8	28.0 ± 27.3	−12.0 ± 24.5	−11.2 ± 27.8	0.66	0.68
Margarine	27.4 ± 21.4	22.3 ± 22.3	1.8 ± 21.6	1.6 ± 21.2	0.56	0.53
Red meat[e]	64.5 ± 40.4	59.8 ± 30.3	−5.4 ± 47.0	−7.1 ± 32.5	0.05	0.03
Poultry	13.4 ± 14.2	14.5 ± 16.9	3.5 ± 13.7	1.4 ± 16.4	0.96	0.97
Sausage	63.4 ± 52.0	55.0 ± 53.5	−19.0 ± 49.4	−18.7 ± 61.9	0.24	0.23
Fish	44.1 ± 28.9	40.5 ± 29.1	8.8 ± 27.6	0.63 ± 29.2	0.24	0.24
Egg	44.6 ± 33.1	40.6 ± 31.8	−1.7 ± 24.5	−12.2 ± 36.9	<0.01	<0.01
Coffee	442 ± 275	530 ± 316	−97.4 ± 273	−81.0 ± 267	0.23	0.34
Sugar	31.0 ± 18.2	26.4 ± 20.0	−2.1 ± 19.1	−11.4 ± 22.5	0.02	0.03

a: Values are means ± SD.

b: Statistical significance is as follows: *, difference between cases and controls in change in food consumption during follow-up calculated by analysis of covariance; †, difference in change in food consumption by analysis of covariance; adjustments were made for age at baseline and age at case-control visit, baseline food consumption value, and supplementation group.

c: Including oat, barley, rice, and corn, but not rye and wheat.

d: Including yogurt and sour milk products.

e: Beef and pork.

Table 2. Daily Nutrient Intake at Case-Control Visit and Change in Daily Nutrient Intake From Baseline to Case-Control Visit[a]

Nutrient	Case-Control Intake		Change in Nutrient Intake		*P* Value for Δ[b]	
	Cases (n = 50)	Controls (n = 3,324)	Cases (n = 50)	Controls (n = 3,324)	Crude	Adjusted
Total energy, kcal[c]	2,899 ± 773	2,549 ± 722	−31.0 ± 668	−265 ± 681	<0.01	<0.01
Protein, g	107 ± 31.4	94.9 ± 27.5	3.42 ± 28.9	−8.45 ± 26.0	<0.01	0.20
Total fat,[d] g	108 ± 33.1	92.8 ± 33.1	−2.96 ± 33.3	−12.8 ± 31.9	<0.01	0.59
Fatty acids, g						
Saturated	51.8 ± 21.1	43.5 ± 19.5	−2.27 ± 18.5	−8.85 ± 18.2	<0.01	0.55
Monounsaturated	37.1 ± 11.4	32.3 ± 11.2	−1.12 ± 10.6	−4.14 ± 11.0	0.01	0.92
Polyunsaturated	14.6 ± 7.10	13.0 ± 7.40	0.55 ± 7.30	0.79 ± 6.81	0.49	0.40
Trans	4.24 ± 2.11	3.35 ± 2.27	0.08 ± 2.52	−0.19 ± 2.20	0.04	0.72
Cholesterol, mg	538 ± 236	475 ± 213	−20.0 ± 180	−105 ± 222	<0.01	0.36
Carbohydrates, g	317 ± 97.8	279 ± 87.9	6.29 ± 87.6	−26.3 ± 82.6	<0.01	0.68
Starch, g	143 ± 49.1	136 ± 48.9	−12.7 ± 45.8	−11.9 ± 47.8	0.78	<0.01
Sucrose, g	72.5 ± 42.3	55.4 ± 34.6	17.0 ± 40.3	−5.14 ± 32.7	<0.01	<0.01
Fiber, g	24.1 ± 9.37	23.6 ± 9.46	−2.33 ± 9.63	−2.31 ± 9.04	0.84	0.05
NCP, g						
Water insoluble	10.6 ± 4.33	10.4 ± 4.45	−1.27 ± 4.66	−1.01 ± 4.41	0.76	0.03
Water soluble	5.41 ± 1.97	5.16 ± 1.90	−0.38 ± 1.87	−0.57 ± 1.78	0.61	0.25
Alcohol, g	17.0 ± 23.6	16.7 ± 21.5	−4.85 ± 14.3	−0.56 ± 18.0	0.23	0.11
β-Carotene, mg	2.21 ± 1.44	2.04 ± 1.55	0.02 ± 1.61	−0.18 ± 1.55	0.34	0.45
Vitamin C, mg	104 ± 56.9	91.5 ± 45.7	3.45 ± 46.3	−17.9 ± 46.2	<0.01	<0.01
Vitamin D, μg	6.54 ± 3.17	5.62 ± 3.14	1.01 ± 3.19	0.14 ± 3.10	0.07	0.59
Vitamin E, mg	13.4 ± 5.51	12.2 ± 5.66	0.08 ± 5.63	−0.004 ± 5.16	0.41	0.26
Calcium, mg	1,566 ± 652	1,256 ± 523	193 ± 652	−128 ± 470	<0.01	<0.01
Iron, mg	17.8 ± 6.38	16.8 ± 5.39	−1.87 ± 5.45	−1.83 ± 5.31	0.41	<0.01

a: Values are means ± SD. NCP, noncellulose polysaccharides.

b: Statistical significance is as follows: *, difference between cases and controls in change in nutrient intake during follow-up calculated by analysis of covariance; †, difference in change in nutrient intake by analysis of covariance; adjustments were made for age at baseline and age at case-control visit, baseline nutrient intake value, total energy intake (not for total energy itself), and supplementation group.

c: 1 kcal = 4.2 kJ.

d: Calculated as triacylglycerides.

risk for colorectal cancer in the case-control analysis, but in the case-cohort analysis no significant associations were observed with food consumption and colorectal cancer risk (data not shown). Table 3 shows the relative risks and odds ratios by nutrient intake. With case-control data, high intakes of total energy and calcium were related to a significantly increased risk for colorectal cancer, whereas the intake of starch, total fiber, water-insoluble fiber (water-insoluble noncellulose polysaccharides), and iron had a significant protective effect. In the case-cohort design, the only statistically significant effect, a protective one, was found with cholesterol intake. All other associations with nutrient intake and risk for colorectal cancer were nonsignificant. However, the intake of polyunsaturated fatty acids and *trans*-fatty acids suggested an apparently harmful effect and the intake of protein, carbohydrates, sucrose, vitamin C, and calcium a protective one, the change in relative risks being >20%.

Discussion

Our finding that the change in diet from baseline to the time of diagnosis differed between cases and controls indicates the potential for serious misclassification. In case-control studies of dietary risk factors for cancer, diet before diagnosis is usually recalled by the patient. Many factors may, however, bias this recall. Most studies have shown the current diet to affect the recalled diet (5,6,20,22). Because persons with cancer may have their own beliefs regarding factors affecting the development of cancer, they may over- or underreport particular food items (31). Recall bias can also arise from factors connected with their general attitude: anxiety and stress induced by the cancer diagnosis, difficulties in memory, and unwillingness to concentrate on dietary questions. However, although studies comparing retrospective with original information on diet have shown differential recall between colorectal cancer patients and their controls (5,6), breast cancer cases and their controls have shown no evidence of recall bias (19,23) or only minor differences in recall (20,21). Alternatively, the undiagnosed colorectal cancer may cause changes in diet during the 12 months before diagnosis.

The time frame of the case-control dietary assessment may affect the dietary outcome. Ideally, the dietary assessment should reflect the period before initiation of cancer, but this is not possible to define. Likewise, it is difficult to determine the appearance of symptoms related to colorectal cancer, because gastrointestinal symptoms are so common. Thus

Table 3. RR for Colorectal Cancer by Case-Cohort (Baseline Data) Nutrient Intake and OR by Case-Control Nutrient Intake and 95% CI[a]

	Case-Cohort		Case-Control	
Nutrient	RR	95% CI	OR	95% CI
Total energy (898 kcal[b])	1.12	0.87–1.43	1.69	1.27–2.26
Protein (34.1 g)	0.57	0.25–1.28	1.21	0.63–2.33
Total fat[c] (39.8 g)	1.00	0.50–2.01	1.05	0.54–2.04
Fatty acids				
Saturated (23.2 g)	0.85	0.50–1.45	0.99	0.62–1.58
Monounsaturated (13.8 g)	0.99	0.51–1.92	1.01	0.52–1.97
Polyunsaturated (8.9 g)	1.22	0.93–1.60	1.06	0.76–1.48
Trans (2.5 g)	1.21	0.95–1.55	1.21	0.91–1.61
Cholesterol (243 mg)	0.53	0.35–0.80	0.96	0.63–1.45
Carbohydrates (111 g)	0.73	0.43–1.22	0.97	0.50–1.90
Starch (59.3 g)	0.98	0.64–1.49	0.57	0.35–0.92
Sucrose (40.2 g)	0.79	0.53–1.18	1.30	0.95–1.78
Fiber (11.6 g)	0.93	0.64–1.36	0.62	0.40–0.98
NCP				
Water insoluble (5.54 g)	0.99	0.70–1.40	0.60	0.38–0.94
Water soluble (2.35 g)	0.85	0.57–1.26	0.68	0.43–1.08
Alcohol (21.8 g)	1.19	0.97–1.48	1.01	0.78–1.32
β-Carotene (1.66 mg)	0.91	0.69–1.20	1.00	0.75–1.34
Vitamin C (52.3 mg)	0.71	0.50–1.00	1.11	0.82–1.51
Vitamin D (3.65 μg)	1.06	0.81–1.40	1.15	0.85–1.56
Vitamin E (6.70 mg)	1.17	0.82–1.69	1.00	0.69–1.43
Calcium (652 mg)	0.79	0.48–1.30	1.57	1.06–2.33
Iron (6.71 mg)	1.02	0.48–2.18	0.51	0.29–0.92

a: Relative risk (RR) was determined by case-cohort analysis and odds ratio (OR) by logistic regression. RR and OR are presented per interquartile range of daily nutrient intake (in parentheses). OR was adjusted for total energy intake (not total energy intake itself), age, and study supplementation group. CI, confidence interval.

b: 1 kcal = 4.2 kJ.

c: Calculated as triacylglycerides.

asking for the diet 12 months before diagnosis was considered most reasonable for this study. This agrees with the design of many other case-control studies as well (32–35).

In our study the fact that the cancer cases reported a significant increase during follow-up in their consumption of fruits and berries, fruit juices, low-fat milk, cream, and cheese and a decrease in their consumption of potatoes compared with controls may have resulted from cancer cases' poor appetite and digestion or from extensive colorectal surgery resulting in intestinal discomfort or food intolerance. This may be reflected in increased consumption of liquid foods (with the exception of coffee), as observed here. Our case selection may have included proportionately more cases who underwent treatment successfully, involving radical surgery, and these cases may have reported healthier diets after surgery.

Cases had a very small decrease in total energy intake over time, whereas controls decreased their total energy intake markedly. In contrast, the mean body mass index of the cases decreased during follow-up, whereas that of the controls remained unchanged. This suggests the possibility that the metabolic rate differed between cancer cases and controls and resulted in less efficient utilization of food energy among cases. This would support the view of a true increase in the energy intake of cancer cases even before diagnosis, as has been reported earlier (36,37).

During follow-up, our controls decreased their food consumption and thus most of their nutrient intake. This could be due to the fact that the dietary questionnaire is easier to complete when the study protocol and the questionnaire are familiar. Thus, in repeated questionnaires, the mean intake tends to decrease because of learning or some other reason (27,38). Another possible explanation in our study is that at the time of the controls' second dietary questionnaire, even with no change in their body mass index, their energy expenditure, because of aging and retirement, was reduced, making the true intake lower than at baseline.

When we were estimating relative risks and odds ratios for dietary risk factors and colorectal cancer, the results differed depending on whether dietary data were used from the case-control or the case-cohort design (baseline data). In the case-control design, an increased risk for colorectal cancer was associated with high total energy and calcium intake, which is in part consistent with earlier findings from case-control studies (32–34,39–42); calcium intake has also been found to be protective in relation to colon cancer (35,43,44). On the other hand, we found no significant effects on the risk for colorectal cancer associated with total energy or calcium intake when the relative risks were calculated in the case-cohort design, and this is consistent with findings from cohort studies (13,45). Similarly, our case-control data indicated a decreased risk for colorectal cancer

in association with total fiber, water-insoluble fiber, and starch intake, as has been shown in many but not in all earlier case-control studies (39), whereas our baseline data indicated no association with intake of starch, total fiber, or water-insoluble fiber. This, too, is consistent with previous cohort studies of fiber and colon cancer (13–15). These results from the present study and previous studies demonstrate consistent differences between case-control and cohort studies in estimating risk associations for several dietary factors. Our finding that cholesterol intake showed a significant protective association in the case-cohort analysis but no effect in the case-control data raises the possibility that the case-control design might not detect an existing relationship, even if dietary cholesterol intake has not been directly related to risk for colorectal cancer previously.

In addition to recall bias, subject selection may affect the results of case-control studies (46). We did not, however, evaluate the effect of subject selection. The participants in the ATBC Study were chronic smokers and willing to participate in a trial of many years, and thus the effects of dropouts and refusals was probably different from that of dropout in another test population. Thus the case-cohort relative risks and case-control odds ratios of this study should not be interpreted as true risk estimates for colorectal cancer in this population; they were presented as examples of how results would change when different diet data were used.

In conclusion, we found considerable differences between colorectal cancer cases and controls in the change in reported dietary habits between study entry and the time of diagnosis. Accordingly, the odds ratios for colorectal cancer using case-control data were markedly different from relative risks based on baseline data. These findings should be taken into consideration when interpreting population-based case-control studies assessing associations between diet and colorectal cancer.

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